Chemical Name: Diphacinone

CAS Number: 82-66-6

PC Code: 067701

Citations:

Teeters, W.R. (1981) Diphacinone technical: Toxicity to Laboratory Rat: Test No. 51. (U.S. Environmental Protection Agency, Pesticides Regulation Div., Agricultural Research Center, Animal Biology Laboratory, unpublished report.)

Teeters, W.R. (1981) Diphacinone technical: Toxicity to Laboratory Rat: Test No. 75. (U.S. Environmental Protection Agency, Pesticides Regulation Div., Agricultural Research Center, Animal Biology Laboratory, unpublished report.)

Purpose of Review: Litigation/Endangered Species

Date of Data Review: 5/15/11

Brief Summary of Study Findings:

<u>Methods</u>

Both studies were conducted in the same lab using very similar methodology. An outline of the available methodology information for each study is provided in **Table 1**.

Table 1. Study methods for the Albino rat feeding studies with diphacinone conducted at Beltsville Lab.		
	Test 51	**Test 75**
Date started	1/16/80	6/20/80
active ingredient	99.9%	
Mixing in feed	Diphacinone mixed with 40 g corn oil, added to mash to make 2000 g of diet	Diphacinone mixed with 40 g corn oil, added to mash to make 2000 g of diet
Species tested	Albino rats	
Test animal weight range	93-120 g	91-120 g
Number of animals per concentration	5 male and 5 female	
Number of control animals	5 male and 5 female	

Table 1. Study methods for the Albino rat feeding studies with diphacinone conducted at Beltsville Lab.		
	Test 51	**Test 75**
Test concentrations	2.1 3.5 5.9 10.0 17.0 mg a.i./kg-diet	0.71 1.21 2.06 3.50 5.95 mg a.i./kg-diet
Length of test	5 days pre-test 5 days treated feed 9 days post-trt	
Environmental conditions	Individually caged, no other laboratory conditions reported	
Variables recorded	Date of death Weight start of pre-treatment Weight start of treatment Weight start of post- treatment Final weight (end of test or at death) Food consumption during each of the three observation intervals	

Results

ToxAnal2009 was used to determine the LC_{50} and slope (if possible) for each of the studies; statistical output at end of data review. These results are reported in Table 2. Test number 75 resulted in the lowest LC_{50} (2.08 mg ai/kg-diet) and will be used for risk estimation.

Table 2. Summary of test results f or the Albino rat feeding studies conducted at Beltsville Lab.		
Test Number	**LC_{50} (95% CI)**	**Probit slope (95% CI)**
51	2.54 (1.79, 3.19) mg a.i./kg-diet	6.7 (2.2,11.2)
75	2.08 (1.57, 2.76) mg a.i./kg-diet	4.2 (2.3, 6.1)

No control animals died during the study. Animals were followed for 14 days after the starting the treated diet (5 days treated diet, followed by 9 days clean diet). All mortalities occurred between days 3 and 12 after the feeding of treated diet started, with a majority of mortalities occurring on days 4, 5, 6, or 7. Although the study reports included data on body weight and food consumption, statistical analysis was not conducted for these parameters because of the high rate of mortality.

Description of Use in Document: Both studies are classified as Supplemental. Data can be used quantitatively in risk assessments, but do not meet any OSCPP 850 series guideline protocols.

Rationale for Use: These are the only available short-term feeding studies for mammals.

Limitations of Study: Details regarding laboratory conditions are not provided. Occurrence of sub-lethal signs of toxicity not reported. Necropsy results not reported.

Reviewer: Christine Hartless, OPP/EFED/ERB2 ——— 5-17-12

Secondary Review: Elizabeth Riley, OPP/EFED/ERB6 5/17/12

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CONC.     NUMBER        NUMBER       PERCENT      BINOMIAL
          EXPOSED       DEAD         DEAD         PROB.(PERCENT)
  17        10            10          100         9.765625E-02
  10        10            10          100         9.765625E-02
  5.9       10            10          100         9.765625E-02
  3.5       10             8           80         5.46875
  2.1       10             3           30         17.1875
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THE BINOMIAL TEST SHOWS THAT 0 AND 5.9 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 2.565211

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD
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    SPAN      G          LC50         95 PERCENT CONFIDENCE LIMITS
    1      .8025485    2.565211      1.155361      3.63299
```

RESULTS CALCULATED USING THE PROBIT METHOD
```
ITERATIONS            G            H           GOODNESS OF FIT PROBABILITY
    6               .445542       1                         .9897495
```

SLOPE   =   6.706074
95 PERCENT CONFIDENCE LIMITS = 2.229841   AND   11.18231

INTERCEPT=-2.721569

LC50 =   2.545871
95 PERCENT CONFIDENCE LIMITS = 1.787613 AND 3.193944

       LC25 =   2.019556
95 PERCENT CONFIDENCE LIMITS = .9898407 AND 2.501664

       LC10 =   1.639555
95 PERCENT CONFIDENCE LIMITS = .5461539 AND 2.137601

       LC05 =   1.447276
95 PERCENT CONFIDENCE LIMITS = .3792486 AND 1.962919
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TNM75

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   CONC.   NUMBER       NUMBER        PERCENT      BINOMIAL
           EXPOSED      DEAD          DEAD         PROB.(PERCENT)
   5.95    10           9             90           1.074219
   3.5     10           10            100          9.765625E-02
   2.06    10           4             40           37.69531
   1.21    10           2             20           5.46875
    .71    10           0             0            9.765625E-02
```

THE BINOMIAL TEST SHOWS THAT .71 AND 3.5 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 2.203218

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD
```
   SPAN      G          LC50         95 PERCENT CONFIDENCE LIMITS
   4        .1687796    1.915214     1.372364     2.594997
```


RESULTS CALCULATED USING THE PROBIT METHOD
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ITERATIONS           G              H            GOODNESS OF FIT PROBABILITY
   4                .1988789        1                         .1868103
```

SLOPE   =   4.230127
95 PERCENT CONFIDENCE LIMITS = 2.343666   AND   6.116588

INTERCEPT=-1.347415

LC50 =   2.082228
95 PERCENT CONFIDENCE LIMITS = 1.574244 AND 2.755374

        LC25 =   1.44237
95 PERCENT CONFIDENCE LIMITS = .9315541 AND 1.861975

        LC10 =   1.036475
95 PERCENT CONFIDENCE LIMITS = .5404182 AND 1.406561

        LC05 =   .8505008
95 PERCENT CONFIDENCE LIMITS = .3847466 AND 1.205881
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